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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/502,259	07/21/2004	Patrick, Arnoldus, Maria Van Buggenum	0-2002.712 US	9811

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ORGANON USA, INC.  
PATENT DEPARTMENT  
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EXAMINER
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BADIO, BARBARA P

ART UNIT	PAPER NUMBER
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1612

MAIL DATE	DELIVERY MODE
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04/01/2008

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/502,259	<b>Applicant(s)</b> VAN BUGGENUM ET AL.	
	<b>Examiner</b> Barbara P. Badio, Ph.D.	<b>Art Unit</b> 1612	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☐ Responsive to communication(s) filed on \_\_\_\_.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-10 is/are pending in the application.  
4a) Of the above claim(s) \_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-10 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. ____. |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date <u>7/21/2004 &amp; 9/26/2007</u> . | 6) <input type="checkbox"/> Other: ____.  |

### **First Office Action on the Merits**

#### ***Priority***

1. If applicant desires to claim the benefit of a prior-filed application under 35 U.S.C. 371, a specific reference to the prior-filed application in compliance with 37 CFR 1.78(a) must be included in the first sentence(s) of the specification following the title or in an application data sheet. For benefit claims under 35 U.S.C. 120, 121 or 365(c), the reference must include the relationship (i.e., continuation, divisional, or continuation-in-part) of the applications.

If the instant application is a utility or plant application filed under 35 U.S.C. 111(a) on or after November 29, 2000, the specific reference must be submitted during the pendency of the application and within the later of four months from the actual filing date of the application or sixteen months from the filing date of the prior application. If the application is a utility or plant application which entered the national stage from an international application filed on or after November 29, 2000, after compliance with 35 U.S.C. 371, the specific reference must be submitted during the pendency of the application and within the later of four months from the date on which the national stage commenced under 35 U.S.C. 371(b) or (f) or sixteen months from the filing date of the prior application. See 37 CFR 1.78(a)(2)(ii) and (a)(5)(ii). This time period is not extendable and a failure to submit the reference required by 35 U.S.C. 119(e) and/or 120, where applicable, within this time period is considered a waiver of any benefit of such prior application(s) under 35 U.S.C. 119(e), 120, 121 and 365(c). A benefit claim

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filed after the required time period may be accepted if it is accompanied by a grantable petition to accept an unintentionally delayed benefit claim under 35 U.S.C. 119(e), 120, 121 and 365(c). The petition must be accompanied by (1) the reference required by 35 U.S.C. 120 or 119(e) and 37 CFR 1.78(a)(2) or (a)(5) to the prior application (unless previously submitted), (2) a surcharge under 37 CFR 1.17(t), and (3) a statement that the entire delay between the date the claim was due under 37 CFR 1.78(a)(2) or (a)(5) and the date the claim was filed was unintentional. The Director may require additional information where there is a question whether the delay was unintentional. The petition should be addressed to: Mail Stop Petition, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

If the reference to the prior application was previously submitted within the time period set forth in 37 CFR 1.78(a), but not in the first sentence(s) of the specification or an application data sheet (ADS) as required by 37 CFR 1.78(a) (e.g., if the reference was submitted in an oath or declaration or the application transmittal letter), and the information concerning the benefit claim was recognized by the Office as shown by its inclusion on the first filing receipt, the petition under 37 CFR 1.78(a) and the surcharge under 37 CFR 1.17(t) are not required. Applicant is still required to submit the reference in compliance with 37 CFR 1.78(a) by filing an amendment to the first sentence(s) of the specification or an ADS. See MPEP § 201.11.

***Claim Rejections - 35 USC § 103***

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

3. Claims 1-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Babcock et al. (US 3,341,557), Campbell et al. (Steroids, 1963) and Loozen et al. (WO 01/05806).

Each of Babcock and Campbell teaches the production of 7 $\alpha$ -methyl derivatives of steroid compounds by reacting the corresponding 4,6-diene-3-ketone compounds with a methyl Grignard reagent, such as methyl magnesium iodide and methyl magnesium bromide, in the presence of a cuprous salt such as cuprous chloride (see each in its entirety, especially see **Babcock**, col. 6, line 71 - col. 7, line 19 and Examples 1, 3, 5, 27 etc.; **Campbell**, paragraph bridging pages 317-318 and Scheme on page 319). Campbell teaches selectivity and good yield of the 7 $\alpha$ - derivatives when Grignard reagent is utilized in the presence of a cuprous salt in the instant process (see page 318, lines 1-4). Babcock teaches solvents such as tetrahydrofuran and ether (see col. 7, lines 4-7); temperature of -40<sup>0</sup>C to the boiling point of the reaction mixture (see col. 7, lines 7-11) and the use of at least five moles of Grignard per mole of steroid (see col. 7, lines 15-17).

The instant claims differ by the recitation of a trialkylsilyl protected starting material in the process taught by each of Babcock and Campbell. However, acyl groups such as acetyl and trialkylsilyl groups such as trimethylsilyl are known hydroxyl protecting groups (see for example **Loozen**, page 5, lines 23-27). Additionally, Loozen teaches 7 $\alpha$ -alkylation of 4,6-diene-3-one steroid derivatives having trialkylsilyl protecting groups (see page 9, example 1) as well as acyl protecting groups (see page 12, example 2). Therefore, the skilled artisan in the art at the time of the present invention would have the reasonable expectation that the protection of the hydroxyl groups in the compounds taught by Babcock and Campbell with a trialkylsilyl group instead of an acetyl group would result in the production of the desired 7 $\alpha$ -alkylation of the prior art compounds.

Claim 3 further differs by reciting CH<sub>3</sub>MgCl. However, CH<sub>3</sub>MgCl is a well known Grignard reagent (see for example, **US 4,298,559**, col. 4, lines 8-19; **US 7,304,157**, col. 13, lines 63-65).

Claim 6 further differs by reciting specific concentrations of steroid of formula (II). However, the court has held that merely selecting proportions and ranges is not patentable absent a showing of criticality. In re Russell, 439 F.2d 1228, 169 USPQ 426 (CCPA 1971).

4. Claim 10 is rejected under 35 U.S.C. 103(a) as being unpatentable over Peters et al. (WO 01/58919).

Peters et al. teaches the syntheses of steroids having anti-estrogenic and other therapeutic properties (see the entire article, especially Abstract). The reference teaches several compounds useful as intermediates in the disclosed syntheses including compounds of formulae XXI (page 20) and XXVIII (page 26 and page 55, claim 8).

The instant claim differs from the reference by reciting a compound not exemplified by the reference. However, Peters exemplifies the acetyl derivative of the instant compound (see figure 4, compound 9) and teaches hydroxymethyl or a protected hydroxymethyl group in the 21-position (see formula XXVIII on page 26 and claim 8 for definition of R<sup>19</sup> group). Therefore, the instantly claimed compound would have been obvious to the skilled artisan in the art at the time of the present invention because he would have had the reasonable expectation that replacing compound 9 with the free alcohol derivative would result in the production of the corresponding free alcohol derivative of compound 10, i.e., compound 11, as set forth in figure 4.

#### ***Other Matters***

5. All references cited by applicant in IDS dated July 21, 2004.

#### ***Telephone Inquiry***

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Barbara P. Badio, Ph.D. whose telephone number is 571-272-0609. The examiner can normally be reached on M-F from 6:30am-4:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Frederick Krass can be reached on 571-272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Barbara P. Badio, Ph.D./  
Primary Examiner, Art Unit 1612